REMARKS

This is a Supplemental Amendment to the Amendment filed on April 16, 2004, which was filed in response to the Office Action mailed November 18, 2003.

Applicants note that the present Amendment includes new claims, amendments to pending claims, amendments to the specification, and remarks regarding the outstanding rejection under 35 U.S.C. § 112, Second Paragraph, and the outstanding rejection under 35 U.S.C. § 102(b) over the Chishima reference (Cancer Research, May 15, 1997; 57:2042-47). The remarks are intended to supercede the remarks presented in the Amendment filed April 16, 2004 with respect to those rejections.

The present Amendment does not include remarks regarding: the priority claim and amendment of the specification to recite the priority information; the objections to the claims, the rejection under 35 USC § 102(a) over the Meng reference; the rejection under 35 U.S.C. § 103(a) over the Meng reference; and the rejection under 35 U.S.C. § 103(a) over the Meng reference, further in view of the Moir reference or the Lubinecki reference. For Applicants' remarks on those topics, Applicants refer the Examiner to the Amendment filed April 16, 2004, at pages 2 and 16 (the priority claim and amendment of the specification to recite the priority information); page 17 (the rejection under 35 USC § 102(a) over the Meng reference); page 18 (the rejection under 35 U.S.C. § 103(a) over the Meng reference); and page 19 (the rejection under 35 U.S.C. § 103(a) over the Meng reference, further in view of the Moir reference or the Lubinecki reference; the objections to the claims).

Applicants thank the Examiner for the courtesy of the brief telephone call held Tuesday June 8, 2004, in which the Examiner confirmed that this amendment would be entered if timely submitted, and suggested that the amendment be filed by facsimile.

Claims 1-6, 8-34 and 36-101 are pending in this application. Claims 1-7, 34-36, and 39-58 are rejected, and claims 8-11, 13-33, 37 and 38 are objected to. By this amendment, claims 1-3, 8, 9, 12, 13, 15-19, 22, 24, 26, 29, 40, 44, 49, and 56 are amended, claims 59-101 are cancelled, and new claims 102-103 are added. Following entry of this amendment, claims 1-6, 8-34, 36-58, and 102-103 will be pending. No new matter is added by the amendments and new claims. Support for the amended and new claims is found throughout the specification and originally filed claims, including, e.g., at page 8, lines 16-18; Figures 1 and 2A; page 27, lines 1-5, 10-11 and 17-18; page 28, lines 3-6; page 3, lines 23-25; page 24, lines 35-40; and originally filed claims 7 and 35.

In addition to the amendments discussed below, Applicants note that claims 2 is amended and now recites "the gene encoding dihydrofolate reductase (DHFR) and the gene encoding glutamine

synthetase" (rather than "the genes encoding dihydrofolate reductase (DHFR) and glutamine synthetase"). This is a non-narrowing amendment. Claims 3, 9, 44, and 56 are amended to recite "gene encoding DHFR" (rather than "DHFR gene") to improve the consistency of claim language. Compare, e.g., claim 2. This is a non-narrowing amendment. Claim 8 is amended to recite "to form a fusion gene" (rather than "as a fusion gene") to improve the consistency of claim language. Compare, e.g., claim 24. This is a non-narrowing amendment. Claims 12 and 13 are amended to delete the phrases "and wherein the fusion gene and selected sequence are operably linked to the promoter 5' of the intron" and "wherein the selected sequence and fusion gene are operably linked to the promoter 5' of the selected sequence", respectively. Applicants submit that the new language is implicit in claims 1 and 8 (from which these claims depend). Claims 15, 16, 17, 19, 22, 26, and 29 are amended to recite "positioned 3' " (rather than "3' ") to improve the consistency of claim language. Compare, e.g., claims 18, 23, 27 and 30. This is a non-narrowing amendment. Claims 15 and 16 are amended to clarify the claims, and now recite "wherein the amplifiable selectable gene is operably linked to the promoter" and "wherein the GFP gene is operably linked to the promoter", respectively. Claim 17 is rewritten in independent form. The claim has been clarified, and now recites "an intron positioned 3' to the first promoter, and a selected sequence positioned 3' to the intron". The new language is implicit in the claim as originally filed. Claim 18 is amended to recite "first intron (rather than "intron in the first transcription unit") and to delete the phrase "in the second transcription unit", in order to improve the consistency of claim language and eliminate repetitive language in the claim. Compare, e.g., claim 17. Claim 19 is amended to correct minor typographical errors. Claim 24 is amended to delete the phrase "wherein the fusion gene is", in order to improve the consistency of claim language. Compare, e.g., claim 27. Claim 49 is amended to recite "green fluorescent protein gene" (rather than "green fluorescent gene") to correct an obvious typographical error and improve the consistency of the claims. Compare, e.g., claim 1. New claim 102 is identical to original claim 35, which was cancelled in the Amendment filed April 16, 2004.

With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any objection and/or rejection made by the Office. Applicants expressly reserve the right to pursue prosecution of any subject matter or embodiments not presently claimed in one or more future or pending continuation and/or divisional applications.

Specification

The specification is amended to replace "Figure 9" with "Figure 1" at page 24, lines 37 and 39; page 27, lines 10, 17, and 35; and page 28, line 6. Applicants submit that these references to "Figure 9" are obvious typographical errors for at least the following reasons. First, the paragraphs in which the correction has been made refer to "structures" and "configurations" of exemplary polynucleotide constructs. Figure 1 shows 9 exemplary construct designs. By contrast, Figure 9 depicts graphs showing "DNase productivity vs. GFP productivity" and "DNase RNA vs. DNase productivity". Second, the corrected sentences in the specification refer to line numbers within the figure. Figure 1 contains 9 numbered lines within the figure. By contrast, Figure 9 shows two graphs and does not have any numbered lines. Thus it is evident that one of ordinary skill would understand that these references to Figure 9 are obvious typographic errors, and that Figure 1 should be referenced instead. Accordingly, no new matter is added by the amendments, and entry of the amendments is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 7 is rejected under 35 U.S.C. § 112, second paragraph because, allegedly, the claim is vague and indefinite. Specifically, the Office Action states that for a fusion gene to be produced, the GFP gene would have to be in frame with a heterologous DNA fragment, thereby encoding a fusion protein. The Office Action further states that the claim could be interpreted to mean that a GFP gene alone is sufficient to encode fusion proteins. Applicants respectfully traverse this rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

As a preliminary matter, Applicant notes that previously pending claim 7 was canceled in the Amendment filed April 16, 2004. New claim 101, submitted herein, recites "[t]he polynucleotide of claim 1, wherein the GFP gene is a GFP-fusion gene". Applicant will address the rejection as applied to claim 7 and as it might be applied to new claim 101.

Applicants respectfully submit that the meaning of the claim is clear. Specifically, the meaning of "GFP gene", as defined in the present application, encompasses a gene that encodes a GFP fusion protein. See, e.g., specification at page 10, lines 14-19; page 11, lines 10-11. Thus, Applicants submit that the claim would not be interpreted to mean that a GFP gene alone is sufficient to encode a fusion gene, as suggested by the Examiner in the Office Action. However, to expedite prosecution and without conceding the propriety of the rejection, new claim 101 recites that "the GFP gene is a GFP-fusion gene",

as suggested by the Examiner. This is a non-narrowing amendment. Withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102(b) "Chishima"

Claims 1-6 and 39-44 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Chishima et al (Cancer Research, May 15, 1997; 57:2042-47) ("Chishima"). The Office Action states that Chishima allegedly teaches "an expression construct where a GFP gene (S65T) is mobilized into a dicistronic expression vector comprising an amplifiable gene (i.e. DHFR) and a gene expressing a desired product." *See* Office Action at page 6. The Kaufman reference (Nucleic Acids Res. (1991) 19(16):4485-4490) ("Kaufman") is cited under MPEP §2131.01 to provide information relating to alleged intrinsic properties of the pED-mtx^r expression construct referenced in Chishima. The Office Action states that Kaufman allegedly teaches that "the pED-mtx^r construct contains a gene encoding a desired product operably linked to a promoter (i.e. B-lactamase gene, Kaufman, at 4487, Fig.1)". *See* Office Action at page 6.

Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

The Examiner has not made a prima facie case of anticipation. A reference anticipates a claim only if it discloses every element of the claim (Scripps Clinic & Res. Found. v. Genentech, inc., 927 F.2d 1565, 1576 (Fed. Cir. 1991)); Richardson v. Suzuki Motor Co., 868 f.2d 1226, 1236 (Fed. Cir. 1989). The absence from the reference of any claimed element negates anticipation (Kloster speedsteel AB v. Crucible Inc., 793 F.2d 1565, 1571 (Fed. Cir. 1986)).

Claims 1 and 40 recite (in part) that the selected sequence is operably linked to either the amplifiable selectable gene or to the GFP gene, and to a promoter. By contrast, the Office Action did not state, and Chishima does not disclose (either alone or as evidenced by Kaufman), that the selected sequence is operably linked to either the amplifiable selectable gene or the GFP gene, and to a promoter. Thus, a prima facie case has not been made because the Office Action has not demonstrated that each and every limitation of the claims is found in Chishima. Withdrawal of this rejection is respectfully requested.

However, to clarify the claims, and without conceding the propriety of the rejection, claims 1 and 40 have been amended. Claim 1 now recites that "the selected sequence is operably linked to a promoter, and wherein the selected sequence and the promoter are (i) operably linked to the amplifiable selectable

gene or (ii) operably linked to the GFP gene". Claim 17 has been amended and also recites this language. Claim 40 now recites that "the selected sequence is operably linked to a promoter, and wherein the selected sequence and the promoter are (i) operably linked to the amplifiable selectable gene or (ii) operably linked to the fluorescent protein gene". No new matter is introduced by the amendment. Applicants respectfully submit that Chishima does not disclose the claimed subject matter (either alone or as evidenced by Kaufman). Accordingly, withdrawal of this rejection is respectfully requested.

SUMMARY

Applicants believe that this application is now in condition for immediate allowance and respectfully requests that the outstanding rejections be withdrawn and this case passed to issue. No new matter has been introduced, and entry of these amendments is respectfully requested. Reconsideration and further examination of the claims is respectfully requested.

The Examiner is invited to contact the undersigned at (650) 667-6222 in order to expedite the resolution of any remaining issues.

Respectfully submitted,
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